

herewith.

REMARKS

Upon entry of the above amendment, claims 3-5, 8-11, 13 and 15 will be pending in the present application. Applicant respectfully submits that the amendments to the claims do not add any new matter within the meaning of 35 USC §132.

**1. Rejection of claims 1-11, 13 and 15-17 under 35 U.S.C. §112,
1st paragraph**

Claims 1-11, 13 and 15-17 are rejected under 35 U.S.C. §112, 1st paragraph because the Examiner alleges that while the specification is enabled for some of the compounds wherein R2 and R3 do not form a ring, R4 is H, R6-R16 are either H or alkyl, cycloalkyl or combine to form a ring such as pyrrolidine, morpholine, azepine, piperazine, or piperadine, the specification is not enabled for 1) "all the other various substituents for the various Rs"; 2) hydrates, solvates, hydrates of salts or solvates of salts of the compounds or tautomers; or 3) "with respect to claims 13 and 15-17, method of treating illness treatable by a PDE4 inhibitor, an airway disorder nor dermatoses."

RESPONSE

With respect to claims 1-2, 6-7 and 16-17 applicant respectfully notes that these claims have been canceled without prejudice, rendering the basis for this rejection moot as to these

claims.

With respect to the remaining claims, applicant respectfully traverses this rejection. The scope of the presently pending claims is fully enabled by the present specification. In particular, applicant respectfully notes that with the cancellation of claims 1-2 and 6-7, applicant has significantly narrowed the scope of the presently pending claims. As a result, the pending compound claims are much closer in scope to those compounds which are exemplified in the present specification as having been synthesized.

Further, applicant has canceled the language directed to hydrates, solvates, hydrates of the salts, solvates of the salts and tautomers from the claims without prejudice. Further, applicant has significantly narrowed the scope of the presently pending method of treatment claims to claim specific disorders which have clear basis in the specification at page 38 of the present specification. These disorders now recited in claim 15 are art-recognized to be treatable by administration of a PDE4 or PDE3/4 inhibitor. Further, applicant has clearly demonstrated at pages 46-47 that the 28 example compounds synthesized have significant PDE 4 and PDE3/4 inhibition properties. As such, a nexus between the presently pending compounds, PDE-inhibition and diseases known to be treatable by administration of a PDE4 or PDE3/4 inhibitor has clearly been demonstrated by applicant.

Accordingly, the presently pending claims are fully enabled by

the present specification because a person of ordinary skill in the art would not require undue experimentation to practice the presently claimed invention. As such, applicant respectfully requests that the Examiner reconsider and withdraw this rejection.

2. Rejection of claims 1-11, 13 and 15-17 under 35 U.S.C. §103(a)

The Official Action states that claims 1-11, 13 and 15-17 are rejected under 35 U.S.C. §103(a) over WO 98/21208 (Gutterer et al.) and WO 98/40382.

RESPONSE

Again, with respect to claims 1-2, 6-7 and 16-17 applicant respectfully notes that these claims have been canceled without prejudice, rendering the basis for this rejection moot as to these claims. With respect to the remaining rejected claims, applicants respectfully traverse this rejection.

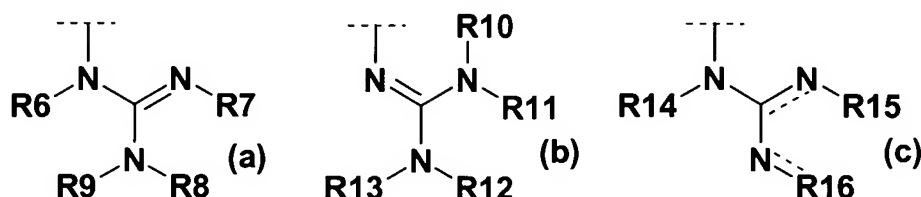
First, applicant respectfully notes that the Examiner has alleged that these two references constitute prior art under 35 U.S.C. §102(e). However, based on the priority date of the present application (August 17, 2002), each of the cited references qualify as prior art under 35 U.S.C. §102(b). In particular, the '208 publication was published May 22, 1998 and the '382 publication was published September 17, 1998. Each date is clearly more than one year older than the present priority date.

To establish a *prima facie* case of obviousness, the PTO must

satisfy three requirements. First, as the U.S. Supreme Court very recently held in *KSR International Co. v. Teleflex Inc. et al.*, 127 S. Ct. 1727, 167 L.Ed. 705 (2007), "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." (*KSR, supra*, slip opinion at 13-15.) Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

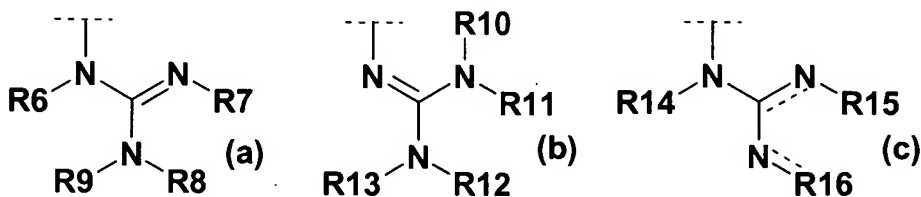
The presently pending claims are not an obvious variation of

the compounds disclosed in the '208 publication. In particular, the '208 publication has absolutely no disclosure of the presently claimed R5 substituent, i.e. formulae (a), (b) and (c):



Further, the '208 publication neither teaches nor suggests how to arrive at the presently claimed compounds which contain formulae (a), (b) or (c).

Similarly, the presently pending claims are not an obvious variation of the compounds disclosed in the '382 publication. In particular, the '382 publication has absolutely no disclosure of the presently claimed R5 substituent, i.e. formulae (a), (b) and (c):



Further, the '382 publication neither teaches nor suggests how to arrive at the presently claimed compounds which contain formulae (a), (b) or (c).

Further, applicant respectfully notes the Examiner's comment at page 11 of the Official Action. The Examiner indicated that "since the prior art compounds are so closely related and the only difference is the substituent on the phenyl, one of skilled in the art would have been motivated to try out other groups at the same position..." (Emphasis Added)

"Motivation to try" is not the standard on which a *prima facie* case of obviousness is based. Instead, the Examiner must show some teaching in a reference which would teach the skilled artisan to arrive at the presently claimed invention. There is no teaching whatsoever in the two cited references which would teach the skilled artisan to arrive at the presently pending claims having the unique and non-obvious R5 substituent.

Further, the Examiner lists two additional US Patents on page 11 of the Official Action: US 6,306,869 and US 6,143,759. It is unclear whether these two patents are part of the rejection or not. Applicant respectfully requests clarification on this point.

In the event that the presently pending claims are rejected over these two patents, applicant respectfully traverses this rejection also. The '869 patent and the '759 patent do not teach the presently claimed R5 substituent as outlined above with the respect to the '208 and '382 publications. Accordingly, none of the cited references identified by the Examiner, taken alone or in combination, teach all of the limitations of the presently pending claims, as required by *In re Wilson*.

Also, the '869 patent discloses a compound which also has an oxygen atom bonded at the same position as R1, further distinguishing it from the presently pending claims. As a result, the presently pending claims are not an obvious variant of the compounds taught in the '869 patent or the '759 patent.

As such, the Examiner has failed to demonstrate a *prima facie* case of obviousness against the presently pending claims. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this rejection of the presently pending claims 3-5, 8-11, 13, and 15.

3. Rejection of claims 1-11, 13 and 15-17 on the grounds of Obviousness-Type Double Patenting

Claims 1-11, 13 and 15-17 have been rejected under the doctrine of obviousness-type double patenting over the following patents:

1. Claims 1-13 of USP 6,008,215;
2. Claims 1-10 of USP 6,306,869;
3. Claims 1-12 of USP 6,143,759; and
4. Claims 1-16 of USP 6,936,622.

RESPONSE

Again, with respect to claims 1-2, 6-7 and 16-17 applicant respectfully notes that these claims have been canceled without prejudice, rendering the basis for this rejection moot as to these

claims. With respect to the remaining rejected claims, applicants respectfully traverse this rejection.

With respect to the remaining claims, applicant respectfully traverses this rejection. However, solely to remove the basis for the rejection of the pending claims over the claims granted in USP 6,936,622, applicant has filed herewith a Terminal Disclaimer over the '622 patent.

Regarding the rejection of the presently pending claims over the '215, '869 and '759 patents, applicant respectfully submits that the presently pending claims are not an obvious variation of the claims contained in these three patents. As outlined above in section 2, the '869 and '759 patents do not fairly teach, nor do they claim, the presently claimed compounds with the unique R5 substituent. The same is true for the '215 patent which does not claim the presently claimed compounds with the unique R5 substituent. Accordingly, the presently claimed compounds are not obvious over the compounds claimed in the '215, '869, and '759 patents, taken alone or in combination, as the R5 substituent of the present claims is not recognized by any of the claims cited by the Examiner, as required by *In re Wilson*.

As such, granting the presently pending claims would not be an unfair extension of patent term of the '215, '869 and '759 patents.

Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this rejection.

CONCLUSION

Based upon the evidence and amendments submitted herewith and the above remarks, the presently claimed subject matter is believed to be novel and patentably distinguishable over the prior art of record. The Examiner is therefore respectfully requested to reconsider and withdraw the pending rejections and allow the presently pending claims to proceed to grant. Favorable action with an early allowance of the claims pending in this application is earnestly solicited.

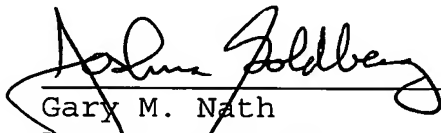
The Examiner is welcomed to telephone the undersigned attorney if she has any questions or comments.

Respectfully submitted,
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